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RECENT SUCCESSES IN TARGETED ANTI-CANCER THERAPY

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A targeted anti-cancer drug works through one or more closely related drug targets that are understood in terms of their epidemiology, pathophysiology and role in the maintenance of the cancer phenotype. Such drugs can be biologics (most frequently monoclonal antibodies), or small molecular weight compounds. The following discussion shall be limited to small molecular weight compounds.

There are now about twenty different and approved targeted anti-cancer drugs on the market, for a wide variety of indications. In molecularly well-defined cancers these drugs show clear benefit and an acceptable tolerability. Limitations of current cancer therapy reside in limited improvement of overall survival, relatively rapid emergence of resistance, limited tolerability and high cost. All of these problems need to be tackled through novel approaches. Novel agents can deal with drug targets that were deemed undruggable until quite recently or that have become resistant to the parent compounds. Judicious combination of two or more agents may help overcoming the emergence of resistance and thereby increase efficacy. Better use of available agents through application of pharmacokinetics-based drug dosing may help to improve tolerability, and the systematic use of pharmacodynamic biomarkers supports patient selection and patient stratification in clinical trials.

ETC has built up all the capabilities to perform state-of-the-art drug discovery while D3, its sister institute is taking care of the downstream activities including preclinical development and early clinical trials, up to and including Proof-of-Concept in man. All of the ETC projects are done in close collaboration with academic institutions in Singapore or overseas, or with industry, on a worldwide basis. Importantly, the academic partner brings deep disease knowledge, the validated drug targets and primary assays to the collaboration.

Two examples shall be discussed that illustrate the approaches taken by ETC and D3 in tackling above-listed issues. The first collaboration with the group of Prof. Tiong S. Ong (Duke-NUS, Singapore) concerns imatinib-resistant chronic myelogenous leukemia while the second one is with Prof. David Virshup (also Duke-NUS) in the field of Wnt inhibitors.